A RESEARCH PROPOSAL

‘’STUDIES OF ORGANOCATALYSTS AND SOME OTHER CATALYTIC SYSTEMS FOR FORMATION OF C-C AND C-N BONDS IN ORGANIC SYNTHESIS”

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STUDIES OF ORGANOCATALYSTS AND SOME OTHER CATALYTIC SYSTEMS FOR FORMATION OF C-C AND C-N BONDS IN ORGANIC SYNTHESIS

INTRODUCTION:

Green chemistry addresses our future challenges in working with chemical processes and products by inventing novel reactions that can maximize the desired products and minimize by-products, designing new synthetic schemes that can simplify operations in chemical productions, and seeking greener solvents that are inherently environmentally and ecologically benign. Hence, the main focus to design synthetic methods that reduce or eliminate the use of toxic substances, washes, solvents and other auxiliaries; it is a tool to minimize the negative impacts of the chemicals and processes involved in the production of the chemicals. Pharmaceutical companies can influence and improve the environmental performance with utilizing green chemistry. Green chemistry is being employed to develop revolutionary drug delivery methods that are more effective and less toxic and could benefit millions of patients.

Sustainability means 'meeting the needs of the present generation without compromising the needs of future generations'. To reach this sustainable development each and everything around the glove are changing rapidly and chemistry is not the exception. Among the various changes and modifications in this subject the keen success has been achieved towards the synthesis of new product and process as the twelve principles of "Green Chemistry" was formulated in 1990s. We the chemists both as academia or industry are trying our level best to follow the twelve principles while doing chemical reactions. If we go through all these twelve principles of green chemistry, it will be seen that the motto of all the principles are same. Thus, keeping all respects in the twelve principles of green chemistry we can express these as 12 D's. Which may be:

1. Decrease of wastes.
2. Designing methods to incorporate maximum starting materials.
3. Designing the products with no or less toxicity.
4. Designing the products with maximum efficacy.
5. Decrease the use of auxiliary substances.

6. Decrease energy requirement of the reactions.
7. Designing synthetic routes using renewable raw materials.
8. Decrease the derivatisation; *e.g.* protections and deprotections.
9. Designing catalytic reactions instead of stoichiometric reagents.
10. Designing biodegradable products.
11. Development of good analytical methodologies.
12. Decrease the probability of accidents by designing the substance and process.

But it is worthy to mention that in preparative purpose if we try to follow all these twelve principles it is next to impossible to carry out a chemical reaction in any laboratory with state-of-the-art infrastructure.

Accordingly, industries from small business to large corporation have already made tactical moves towards sustainability by adopting the key element of green chemistry. Organic synthesis, experienced thoughtful changes in recent years with more sustainable processes that avoid the extensive use of toxic and hazardous solvents and reagents, vigorous reaction conditions, costly and complicated catalytic systems. Solvent-less technology has a number of advantages from the viewpoint of both academy and industry. Two of twelve principles of "Green Chemistry" are to "use of safer solvent and reactions condition" and to "prevent waste". These principles are both directly met by eliminating a reaction medium. Solvent-free and/or solvent-less protocol3 frequently display remarkable rate acceleration due to the increased reaction conditions with some occurring under ambient situation *i.e.* at room temperature, microwave irradiation, ball milling. The poisonous and volatile nature of many organic solvents particularly chlorinated hydrocarbon that are commonly used in huge amounts for organic reaction have created a serious warning to the human health and environment. Thus, propose of solvent-less catalytic reaction has gained undisputed attention in recent times in the area of green synthesis. A solvent-free reaction may be carried out by using the reactants alone or incorporating them with other catalyst to attain high degree of stereo selectivity in the product, to reduce by-product, to maximize rate of reaction. The earlier notion is that 'no reaction is possible without the use of solvent' is now no more applicable. It has been observed that a large number of reactions happened in solid state without use of any solvent. In fact, in a number of cases, such reactions take place more efficiently and more selectivity contrast to reactions carried out in

solvents. Such reactions are simple to handle, reduce pollution, comparatively economical to operate and especially important in industries. It is understood that solvent-free organic syntheses and transformations are industrially constructive and largely green. The advantages of solvent-free reactions are:

(a) Economic (cost saving, save money on solvent).

b) Not required to collect, purify, recycle and remove solvent after completion of reaction.

(c) Due to more availability of reactants reaction rate is generally high *i.e.* reduces reaction time.

(d) Environmentally friendly.

(e) Decreased energy consumption.

(f) Large reduction in batch size volume (reactor size) and capital investment.

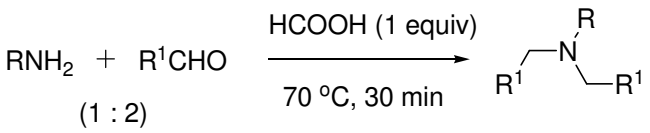
It has been an interesting observation that due to the demerit related with those reactions carried out in conventional organic solvents; synthetic chemists are paying more interest to the development of new methodologies based on solvent-free conditions. The literature based on neat reaction without any catalyst has skilled exponential expansion over the last decades. So, it is very difficult to maintain with the research accounted in this field. Therefore, review literature has become increasingly important to researchers who are trying to keep up with this field. Though all modifications are important and demand their own merit but the concept of "the best solvent is no solvent' is a step forward in the field synthetic chemistry and an alternative approach using solid support is another outcome. Unfortunately, solid support reactions do not entirely meet the definition of no solvent as appreciable amount of solvent is still required for adsorption of reactants and elution of products at the pre and post reaction stages respectively. When we are not using any medium or solvent the term 'neat reaction' has been coined. According to recent literature there are two type of neat reaction ande we can classify as neat reaction Type 1: where there is no solvent as well as no catalysts and Neat reaction Type II where there is no solvent but there is catalyst.

OBJECTIVE:

I would like to work on various aspects to develop more efficient and mild technologies in organic synthesis using different catalytic systems. Some simple and small organic molecule like proline, formic acid, pyridine can act as organocatalyst in various reactions in organic synthesis. Now, it has been established that the use of organocatalysts provide many advantages over conventional metal catalysts. Zwitterionic - type molten salt and task specific ionic liquid are widely used as organocatalysts for organic synthesis. I am interested to develop mild, cost effective and environmentally friendly catalytic systems which will emerge as potential catalyst system for some important transformations in organic synthesis involving C-C and C-N bond.

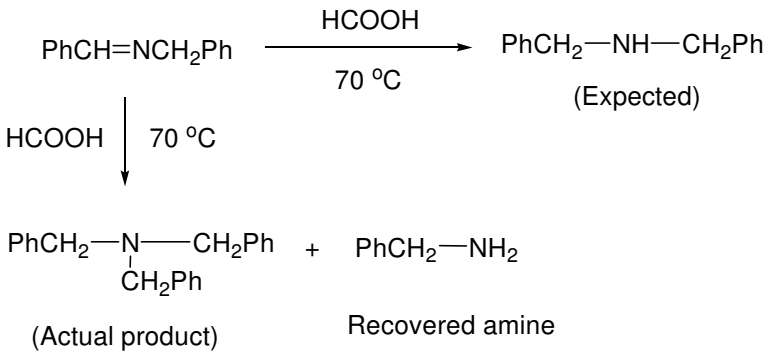
PROPOSED WORK:

The reductive amination of aldehydes and ketones is an attractive procedure on organic synthesis for the C–N bond formation reaction. Reductive alkylation of ammonia/amine or reductive amination of carbonyl compounds is the reaction of carbonyl compounds with ammonia/primary amine/secondary amines. In the reductive amination the choice of reducing agent plays an important role in the success of the reaction in which the imine intermediates need to be reduced selectively over the aldehydes under the same reaction conditions. Traditionally, the reductive amination of aldehydes is carried out using stoichiometric amounts of reducing agents such as borohydrides, formates, silanes and many other different reagents. The development of convenient methods for the synthesis of sterically hindered tertiary amines have gained much attention from the synthetic chemists in recent decades. In literature three methods were reported for the synthesis of sterically hindered tertiary amines such as method involving benzyne intermediates, method involving reactive organometallic reagents and involving cross-coupling reactions. Some other efficient methods were also developed. In continuation of our research to develop the new methodologies in organic synthesis we have improved this procedure to synthesize the sterically hindered tertiary amines selectively with a variety of aldehydes and primary amines using commercially available formic acid as reducing agent.



Scheme 1

OUR PROPOSED METHODOLOGY:



Scheme 2

From the results we assumed that HCOOH initially at lower temperature breaks (hydrolysis) certain imines to produce the carbonyl compounds and amines but at higher temperature the undissociated imines may reduce to the corresponding secondary amine. After hydrolysis the corresponding carbonyl compounds combine with reduced secondary amine to yield the iminium ion which gets reduced by $HCOO^-$ to furnish the corresponding tertiary amine.

ADVANTAGES:

- It is organic solvent free condition
- Metal free
- Easily accessible reactants
- The reaction should be fast
- Simple operation
- General applicability
- Modular nature
- We should get very clear product
- Environmentally friendly reaction conditions

CONCLUSIONS:

In conclusion we have proposed to synthesize selectively sterically hindered tertiary amines as well as some secondary amines based on the Eschweiler-Clarke procedure. In the Eschweiler-Clarke procedure use of formaldehyde was the only variation to prepare the

monomethylated or dimethylated amines. In our proposed methodology we will investigate for the preparation of a variety of tertiary amines by changing both the amines as well as aldehydes.

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